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SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMM		Attorney Docket No.	50125/102001
(MODIFIED)	PATENT AND TRADEMARK OFFICE	Serial No.	10/540,958
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)		Filing Date	January 3, 2006
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(37 C.F.R. § 1.98(b))		IDS Filed	April 8, 2010

		U.S. PATE	NT DOCUMENTS
Examiner's Initials	Document Number	Publication Date	Patentee or Applicant
	5,518,735	May 21, 1996	Stürzebecher et al.
	5,602,253	Feb. 11, 1997	Antonsson et al.
	5,705,487	Jan. 06, 1998	Schacht et al.
	5,707,966	Jan. 13, 1998	Schacht et al.
	5,710,130	Jan. 20, 1998	Schacht et al.
	5,726,159	Mar. 10, 1998	Schacht et al.
	5,863,929	Jan. 26, 1999	Klimkowski et al.
	5,914,319	Jun. 22, 1999	Schacht et al.
	6,030,972	Feb. 29, 2000	Böhm et al.
	6,472,393	Oct. 29, 2002	Aliagas-Martin et al.
	6,586,405	Jul. 01, 2003	Semple et al.
	6,624,169	Sep. 23, 2003	Wilhelm et al.
	6,831,196	Dec.14, 2004	Stürzebecher et al.
	6,841,702	Jan. 11, 2005	Magdolen et al.
	7,038,074	May 2, 2006	Moroder et al.
	7,049,460	May 23, 2006	Magdolen et al.
	7,208,521	Apr. 24, 2007	Magdolen et al.
	7,407,982	Aug. 5, 2009	Steinmetzer et al.
	7,538,216	May 26, 2009	Speri
	7,608,623	Oct. 27, 2009	Speri et al.

EXAMINER	/Marcos Sznaidman/	DATE CONSIDERED	12/02/2010
	citation considered. Draw line through citation	n if not in conformance and not	considered. Include copy of this

SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE		Attorney Docket No.	50125/102001
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INCODE TOUR	1001 001 IDE	Applicant	Stürzebecher et al.
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(37 C.F.R. § 1.98(b))		IDS Filed	April 8, 2010

	U.S. PAT	ENT DOCUMENTS
2004/0266766	Dec. 30, 2004	Speri
2005/0119190	Jun. 2, 2005	Stürzebecher et al.
2005/0176993	Aug. 11, 2005	Stürzebecher et al.
2006/0068457	Mar. 30, 2006	Ziegler et al.
2007/0055065	Mar. 8, 2007	Stürzebecher et al.
2007/0066539	Mar. 22, 2007	Stürzebecher et al.
2008/0261998	Oct. 23, 2008	Speri et al.
2009/0117185	May 7, 2009	Steinmetzer et al.
2010/0022781	Jan. 28, 2010	Steinmetzer et al.

	FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION				
Examiner's Initials	Document Number	Publication Date	Country or Patent Office	Translation (Yes/No	
	CA 2412181	Dec. 9, 2002	Canada		
	CH 689 611	Jul. 15, 1999	Switzerland	Abstract	
	DE 100 29 014	Dec. 20, 2001	Germany	Abstract	
	DE 100 29 015	Dec. 20, 2001	Germany		
	DE 102 10 590	Mar. 11, 2002	Germany		
	DE 102 12 555	Sep. 25, 2003	Germany	Abstract	
	DE 103 01 300	Jul. 29, 2004	Germany	Abstract	
	DE 42 43 858	Jun. 30, 1994	Germany	Abstract	
	EP 0 183 271	Jun. 04, 1986	EPO		

EXAMINER	/Marcos Sznaidman/	DATE CONSIDERED	12/02/2010
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	FOREIGN	PATENT OR PUBLISH	ED FOREIGN PATENT APPLICATION	
	EP 0 669 317	Aug. 30, 1995	EPO	
	EP 0 672 658	Sep. 20, 1995	EPO	
	EP 1 364 960	Nov. 26, 2003	EPO	
	WO 92/08709	May 29, 1992	WIPO	Abstract
	WO 94/18185	Aug. 18, 1994	WIPO	Abstract
	WO 94/29336	Dec. 22, 1994	WIPO	
	WO 95/17885	Jul. 06, 1995	WIPO	
	WO 95/29189	Nov. 02, 1995	WIPO	
	WO 96/25426	Aug. 22, 1996	WIPO	Abstract
	WO 97/23499	Jul. 3, 1997	WIPO	
	WO 99/05096	Feb. 4, 1999	WIPO	
	WO 00/04954	Feb. 3, 2000	WIPO	Abstract
	WO 00/05245	Feb. 3, 2000	WIPO	
	WO 00/14110	Mar. 16, 2000	WIPO	
	WO 00/17158	Mar. 30, 2000	WIPO	Abstract
	WO 00/58346	Oct. 5, 2000	WIPO	
	WO 00/64470	Nov. 2, 2000	WIPO	
	WO 01/81314	Nov. 1, 2001	WIPO	
	WO 01/96286	Dec. 20, 2001	WIPO	
	WO 01/96366	Dec. 20, 2001	WIPO	
	WO 01/97794	Dec. 27, 2001	WIPO	Abstract
	WO 02/06280	Jan. 24, 2002	WIPO	
XAMINER	/Marcos S	naidman/	DATE CONSIDERED 12/02/20	010
	WO 01/97794 WO 02/06280 /Marcos S	Dec. 27, 2001 Jan. 24, 2002 znaidman/	WIPO WIPO	010

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with the next communication to applicant.

	SUBSTITUTE FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	Attorney Docket No.	50125/102001
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FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION			
WO 02/14349	Feb. 21, 2002	WIPO	
WO 02/20475	Mar. 14, 2002	WIPO	
WO 02/50056	Jun. 27, 2002	WIPO	
WO 03/70229	Aug. 28, 2003	WIPO	Abstract
WO 04/062657	Jul. 29, 2004	WIPO	

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)
Asghar et al., "Human Plasma Kallikreins and their Inhibition by Amidino Compounds," Biochim. Biophys. Acta 438:250-264 (1976).
Baker et al., "Inhibition of Cancer Cell Urokinase Plasminogen Activator by its Specific Inhibitor PAI-2 and Subsequent Effects on Extracellular matrix Degradation," Cancer Research 50: 4676-4684 (1990).
Bauer, "Hilfsstoffe," in <i>Pharmazeutische Technologie</i> . Sucker et al. (eds.), Georg Thierne Verlag Stuttgart: New York, p. 174-216 (1991).
Bookser et al., "Syntheses of Quadruply Two-and Three-Atom, Aza-Bridged, Cofacial Bis (5,10,15,20- Tetraphenylporphyrins)," J. Am. Chem. Soc. 113:4208-4216 (1991).
Cajot et al., "Plasminogen-Activator Inhibitor Type 1 is a Potent Natural Inhibitor of Extracellular Matrix Degradation by Fibrosarcoma and Colon Carcinoma Cells," Proc. Natl. Acad. Sci. USA 87:6939-6943 (1990).
Choi-Sledeski et al., "Discovery of an Orally Efficacious Inhibitor of Coagulation Factor Xa Which Incorporates a Neutral P ₁ Ligand," <i>J. Mod. Chem.</i> 46:681-684 (2003).
Collen et al., "In Vivo Studies of a Synthetic Inhibitor of Thrombin," J. Lab. Clin. Med. 99:76-83 (1982).
Coussens et al., "Matrix Metalloproteinase Inhibitors and Cancer: Trials and Tribulations," Science 295:2387-2392 (2002).
Dexter et al., "N/N-Dimethylformamide-induced Alteration of Cell Culture Characteristics and Loss of Tumorigenicity in Cultured Human Colon Carcinoma Cells," Cancer Res. 39:1020-1025 (1979).
Dixon, "The Determination of Enzyme Inhibitor Constants," Biochem. J. 55:170-171 (1953).

EXAMINER	/Marcos Sznaidman/	DATE CONSIDERED	12/02/2010
EXAMINER: Initial citation considered. Draw line through citation form with the next communication to applicant.		tion if not in conformance and not	t considered. Include copy of this

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ı			Group	1612
l	(37 C.F.R. § 1.98(b))		IDS Filed	April 8, 2010

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)
Duggan et al., "Urokinase Plasminogen Activator and Urokinase Plasminogen Activator Receptor in Breast Cancer," Int. J. Cancer 61:597-600 (1995).
Enyedy et al., "Structure-Based Approach for the Discovery of Bis-benzamidines as Novel Inhibitors of Matriptase," J. Med. Chem. 44:1349-1355 (2001).
Eriksson et al., "The Direct Thrombin Inhibitor Melagatran Followed by Oral Ximelagatran compared with Enoxaparın for the Prevention of Venous Thromboembolism after Total Hip or Knee Replacement: the EXPRESS study." <i>Journal of Thrombols</i> and <i>Heemostasis</i> , 1:2490-2496 (2003).
Fareed, et al., "Inhibition of Serine Proteases by Low Molecular Weight Peptides and Their Derivatives", Ann. N. Y. Acad. Sci. 370:765-784 (1981).
Francis et al., "Comparison of Ximelagatran with Warfarin for the Prevention of Venous Thromboembolism after Total Knee Replacement," N. Engl. J. Med. 349:1703-1712 (2003).
Frérot et al., "PyBOP® and PyBroP: Two reagents for the difficult coupling of the q,q-dialkyl amino acid, Aib," Tetrahedron, 47(2):259-270 (1991).
Friedrich et al., "Catalytic Domain Structures of MT-SP1/Matriptase, a Matrix-degrading Transmembrane Serine Proteinase," J. Biol. Chem. 277:2160-2168 (2002).
Garrett et al., "Peptide Aldehyde Inhibitors of the Kallikreins: An Investigation of Subsite Interactions with Tripeptides Containing Structural Variations at the Amino Terminus," J. Pept. Res. 52:60-71 (1998).
Griffin, "Role of Surface in Surface-Dependent Activation of Hageman Factor (Blood Coagulation Factor XII)", Proc. Natl. Acad. Sci. USA 75:1998-2002 (1978).
Garrett et al., "Synthesis of Potent and Selective Inhibitors of Human Plasma Kallikrein," Bioorg. Med. Chem. Lett. 9:301-306 (1999).
Gustafsson et al., "Effects of Melagatran, a New Low-Molecular-Weight Thrombin Inhibitor, on Thrombin and Fibrinolytic Enzymes," <i>Thromb. Haemost.</i> 79:110-118 (1998).
Gustafsson et al., "Effects of Inogatran, A New Low-Molecular-Weight Thrombin Inhibitor, in Rat Models of Venous and Arterial Thrombosis, Thrombolysis and Bleeding Time," <i>Blood Coagulation and Fibrinolysis</i> 7:69-79 (1996)
Gustafsson et al., "The Direct Thrombin Inhibitor Melagatran and Its Oral Prodrug H 376/95: Intestinal Absorption Properties, Biochemical and Pharmacodynamic Effects," <i>Thromb. Res.</i> 101:171-181 (2001).
Gustafsson et al., "A New Oral Anticoagulant: The 50-Year Challenge," Nature Reviews Drug Discovery 3:649-659, 2004.

EXAMINER	/iviarcos Sznaioman/	DATE CONSIDERED	12/02/2010
	citation considered. Draw line through citation	on if not in conformance and no	t considered. Include copy of this

SUBSTITUTE FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	Attorney Docket No.	50125/102001
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		Group	1612
(37 C.F.R. § 1.98(b))		IDS Filed	April 8, 2010

	OTHER DOCUMENTS (INCLUDING AUTHO	OR, TITLE, DATE, PLACE OF F	PUBLICATION)
	Hara et al., "DX-9065a, a New Synthetic, Potent Haemost. 71:314-319 (1994).	Anticoagulant and Selective In	nhibitor for Factor Xa,* <i>Thromb</i> .
	Herbert et al., *DX 9065A, a Novel, Synthetic, Sr Vivo Studies,* J. Pharmacol. Exp. Ther. 276:103		itor of Factor Xa: In Vitro and In
	Ho et al., "Exploratory Solid-Phase Synthesis of Heterocyclic Amides as Novel Types of Non-Bas (1999).	Factor Xa Inhibitors: Discovery sic Arginine Surrogates,* <i>Bioor</i>	y and Application of P ₃ - g. Med. Chem. Lett. 9:3459-3464
	Hooper et al., "Type II Transmembrane Serine F	roteases," J. Biol. Chem. 276:8	857-860 (2001).
	Ihara et al., "Prometastatic Effect of N-Acetylglu- Active Matriptase by Adding β1-6 GlcNAc Brand		
	Isobe, "Inhibitory Effect of Gabexate (FOY) on C	ontact System," Blood & Vesse	9/ 12:135-138 (1981).
	Judkins et al., "A Versatile Synthesis of Amidine 4351-4367 (1996).	s from Nitriles Via Amidoximes	," Synthetic Communications 26:
	Kang et al., "Tissue Microarray Analysis of Hepa for Met, Matriptase, and Hepatocyte Growth Fac Breast Cancer," <i>Cancer Res.</i> 63:1101-1105 (20)	tor Activator Inhibitor 1 in the F	
	Kaplan, "Initiation of the Intrinsic Coagulation an Factor, Prekallikrein, High Molecular Weight Kin (1978).	d Fibrinolytic Pathways of Man inogen, and Factor XI,* <i>Prog. F</i>	: The Role of Surfaces, Hageman Hemostasis Thromb. 4:127-175
	Kettner et al., "Inactivation of Trypsin-Like Enzyr Enzymology 80:826-843 (1981).	nes with Peptides of Arginine (Chloromethyl Ketone," Methods in
	Kettner et al., *The Selective Inhibition of Throm 18297 (1990).	bin by Peptides of Boroarginine	e," J. Biol. Chem. 265, 18289-
	Kettner et al., "The Selective Affinity Labeling of Thromb. Res. 22:645-652 (1981).	Factor X _a by Peptides of Argini	ine Chloromethyl Ketone,"
	Kim et al., "Preparation of Argatroban Analog Tr Studies of Their Cell Permeability and Antithrom	rombin Inhibitors with Reduced botic Activities," Med. Chem. R	d Basic Guanidine Moiety, and Res. 377-383 (1996).
	Kirk, "4-Lithio-1-Tritylimidazole as a Synthetic Int Heterocyclic Chem. 22:57-59 (1985).	termediate, Synthesis of Imidaa	zole-4-Carboxaldehyde," .J.
	Kruger et al., "Host TIMP-1 Overexpression Con Fibrosarcoma Cell Line," Oncogene 16:2419-24		al Brain Metastasis of a
EXAMINER	/Marcos Sznaidman/	DATE CONSIDERED	12/02/2010

Sheet 7 of 12

	SUBSTITUTE FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE	Attorney Docket No.	50125/102001
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			Group	1612
	(37 C.F.R. § 1.98(b))		IDS Filed	April 8, 2010

 OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)
Kruger et al., "The Bacterial LacZ Gene: An Important Tool for Metastasis Research and Evaluation of New Cancer Therapies," Cancer and Metastasis Reviews 17:285-294 (1939).
Künzel et al., "4-Amidinobenzylamine-Based Inhibitors of Urokinase," Bioorg. Med. Chem. Lett. 12:645-648 (2002).
Lawson et al., "Studies on the Inhibition of Human Thrombin: Effects of Plasma and Plasma Constituents Folia Haematol," Leipzig 109, 52-60 (1982).
Leadley, "Coagulation Factor Xa Inhibition: Biological Background and Rationale," Curr. Topics in Med. Chem., 1: 151-159 (2001).
Lee et al., "Noncovalent Tripeptidic Thrombin Inhibitors Incorporating Amidrazone, Amine and Amidine Functions at P1," Bioorg. Med. Chem. Lett. 12:1017-1022 (2002).
Lee et al., "Noncovalent Thrombin Inhibitors Incorporating an Imidazolylethynyl P1," Bloorganic & Medicinal Chemistry Letters, 10:2775-2778 (2000).
Lee et al., "Activation of Hepatocyte Growth Factor and Urokinase/Plasminogen Activator by Matriptase, an Epithelial Membrane Serine Protease," J. Biol. Chem. 275:36720-36725 (2000).
Lin et al., "Characterization of a Novel, Membrane-bound, 80-kDa Matrix-degrading Protease from Human Breast Cancer Cells," J. Biol. Chem. 272:9147-9152 (1997).
Lin et al., "Molecular Cloning of cDNA for Matriptase, a Matrix-degrading Serine Protease with Trypsin-like Activity," J. Biol. Chem. 274:18231-18236 (1999).
Lin et al., "Purification and Characterization of a Complex Containing Matriptase and a Kunitz-type Serine Protease Inhibitor from Human Milk," <i>J. Biol. Chem.</i> 274:18237-18242 (1999).
Long et al., "Synthesis and Evaluation of the Sunflower Derived Trypsin Inhibitor as a Potent Inhibitor of the Type II Transmembrane Serine Protease, Matriptase," Bioorg. Med. Chem. Lett. 11:2515-2519 (2001).
Maduskule et al., "Rational Design and Synthesis of Novel, Potent Bis-Phenylamidine Carboxylate Factor Xa Inhibitors," <i>J. Med. Chem.</i> 41:53-62 (1998).
Maignan et al., "The Use of 3D Structural Data in the Design of Specific Factor Xa Inhibitors," Curr. Topics in Med. Chem. 1:161-174 (2001).
Mignatti et al., "Biology and Biochemistry of Proteinases in Tumor Invasion," <i>Physiological Reviews</i> 73:161-195 (1993).
Mohan et al., "Solid-Phase Synthesis of N-Substituted Amidinophenoxy Pyridines as Factor Xa Inhibitors," Bioorg. Med. Chem. Lett. 8:1877-1882 (1998).

ĺ	EXAMINER	/Marcos Sznaidman/	DATE CONSIDERED	12/02/2010
		al citation considered. Draw line through citation to applicant.	n if not in conformance and no	considered. Include copy of this

SUBSTITUTE FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	Attorney Docket No.	50125/102001
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		Filing Date	January 3, 2006
		Group	1612
		IDS Filed	April 8, 2010

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)
Morrissette et al., "Low Molecular Weight Thrombin Inhibitors With Excellent Potency, Metabolic Stability, and Oral Bioavailability," Bioorganic & Med. Chem. Letters, 14:4161-4164 (2004).
Muramatu et al., "Inhibitory Effects of ω-Amino Acid Esters on Trypsin, Plasmin, Plasma Kallikrein and Thrombin," <i>Biochim. Biophys. Acta</i> 242::203-208 (1971).
Muramatu et al., "Inhibitory Effects of ω-Guanidino Acid Esters on Trypsin, Plasmin, Plasma Kallikrein and Thrombin," <i>Biochim. Biophys. Acta</i> 268:221-224 (1972).
Muramatu et al., "Inhibitory Effects of Anyl trans-4 (Aminomethyl) Cyclohexanecarboxylate on Serine Proteases, and their Antiallergic Effects," Hoppe-Seyler's Z. Physiol. Chem. 363:203-211 (1982).
Nar et al., "Structural Basis for Inhibition Promisculty of Dual Specific Thrombin and Factor Xa Blood Coagulation Inhibitors," Structure, 9:29-37 (2001).
Nelson et al., "Stereoselective Synthesis of a Potent Thrombin Inhibitor by a Novel P2-P3 Lactone Ring Opening," J. Org. Chem. 69:3620-3627 (2004).
Oberst et al., "Expression of the Serine Protease Matriptase and Its Inhibitor HAI-1 in Epithelial Ovarian Cancer: Correlation with Clinical Outcome and Tumor Clinicopathological Parameters," Clin. Cancer Res. 8:1101-1107 (2002).
Ohno et al., "FOY: [Ethyl-(6-Guanidinohexanoyloxy) Benzoate] Methanesulfonate as a Serine Proteinase Inhibitor. I. Inhibition of Thrombin and Factor Xa in Vitro," <i>Thromb. Res.</i> 19:579-588 (1980).
 Okada et al., "Development of Plasmin and Plasma Kallikrein Selective Inhibitors and their Effect on M1 (Melanoma) and ht29 Cell Lines," Bloorg. Med. Chem. Lett. 10:2217-2221 (2000).
Okada et al., "Development of Plasma Kallikrein Selective Inhibitors," Biopolymers 51:41-50 (1999).
Okamoto et al., "Recent Studies of the Synthetic Selective Inhibitors; With Special Reference to Non-Plasmin Fibrinolytic Enzyme, Plasmin and Plasma-Kallikrein Thromb," Res., Suppl. I, 131-141 (1988).
 Ossowski et al., "Antibodies to Plasminogen Activator Inhibit Human Tumor Metastasis," Cell 35:611-619 (1983).
 Ostrem et al., "Discovery of a Novel, Potent, and Specific Family of Factor Xa Inhibitors via Combinatorial Chemistry," <i>Biochemistry</i> 37:1053-1059 (1998).
Patani et al., "Biolsosterism: A Rational Approach in Drug Design." Chem. Rev. 96:3147-3176 (1996), pages 3147-3148 and 3170.
Pauls et al., "The Design of Competitive, Small-Molecule Inhibitors of Coagulation Factor Xa," Frontiers in Med. Chem., 1:129-152 (2004).

EXAMINER	/Marcos Sznaidman/	DATE CONSIDERED	12/02/2010
	tial citation considered. Draw line through citatio ext communication to applicant.	n if not in conformance and no	ot considered. Include copy of this

SUBSTITUTE FORM PTO-1449 (MODIFIED)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	Attorney Docket No.	50125/102001
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		Group	1612
(37 C.F.R. § 1.98(b))		IDS Filed	April 8, 2010

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)
Pedersen et al., "Prognostic Impact of Urokinase, Urokinase Receptor, and Type 1 Plasminogen Activator Inhibitor in Squamous and Large Cell Lung Cancer Tissue" Cancer Research 54:4671-4675 (1994).
Perzborn et al., "In Vitro and In Vivo Studies of the Novel Antithrombotic Agent BAY 59-7939—an Oral, direct Factor Xa Inhibitor," J. Thromb. & Haemost. 3:514-521 (2005).
Phillips et al., "Discovery of N-[2-[5-[Amino(mino)methyl]-2-hydroxyphenoxy]-3,5-difluoro-6-[3-(4,5-dihydro-1-methyl-1H-imidazol-2-ylphenoxy]pyridin-4-ylp-N-methylghydne (2K-807834). A Potent, Selective, and Orally Active Inhibitor of the Blood Coagulation Enzyme Factor (xi. V. Med. Chem. 41:3557-3582 (1998)).
Quan et al., "Bisbenzamidine Isoxazoline Derivatives as Factor Xa Inhibitors," Bloorg. Med. Chem. Lett. 7:2813-2818 (1997).
Quan et al., "Discovery of 1-{3'-Aminobenzisoxazot-5'-yi}-3-trifluomethyl-H-{2'-Iluoro-4-[(2'-dimethylaminomethyl)dimdazot-1-yi]phenyl-1-ft-pyrazote-5-carboxyamide hydrochloride (Razaxaban), a Highly Polent, Selective, and Chaig blicavaliable Teach ox Inhibitor, J. Med. Chem. 48:1729-1744 (2005).
Quan et al., "The Race to Orally Active Factor Xa Inhibitor: Recent Advances," Curr. Opin. In Drug Discovery & Development, 7:460-469 (2004).
Ratnoff, "Studies on the Inhibition of Ellagic Acid-Activated Hageman factor (factor XII) and Hageman factor fragments," <i>Blood</i> 57:55-58 (1981).
Renatus et al., "Structural and Functional Analyses of Benzamidine-based Inhibitors in Complex with Trypsin: Implications for the Inhibition of Factor Xa, tPA, and Urokinase." J. Med. Chem. 41:5445-5458 (1998).
Reuning et al., "Multifunctional Potential of the Plasminogen Activation System in Tumor Invasion and Metastasis (Review)," International Journal of Oncology 13:893-906 (1998).
Rittle et al., "Unexpected Enhancement of Thrombin Inhibitor Potency with o-Aminoalkylbenzylamides in the P1 Position," <i>Bioorg. Med. Chem. Lett.</i> 13:3477-3482 (2003).
Robinson et al., "Chapter 9. Anticoagulants: Inhibitors of the Factor VIIa/Tissue Factor Pathway," Ann. Rep. Med. Chem. 37:35-94 (2002).
Rubini et al., "Synthesis of Isosteric Methylene-oxy Pseudopeptide Analogues as Novel Amide Bond Surrogate Units." Tetrahedron 43(21):6039-6045 (1986)."
Sato et al., "Antithrombotic Effects of YM-60828, a Newly Synthesized Factor Xa Inhibitor, in Rat Thrombosis Models and Its Effects on Bleeding Time," Br. J. Pharmacol. 123:92-96 (1998).
Sato et al., "YM-60828, a Novel Factor Xa Inhibitor: Separation of its Antithrombotic Effects from its Prolongation of Bleeding Time," Eur. J. Pharmacol. 339:141-146 (1997).

EXAMINER	/Marcos Sznaidman/	DATE CONSIDERED	12/02/2010
EXAMINER: Initial citation considered. Draw line through citation		n if not in conformance and not	considered. Include copy of this

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(37 C.F.R. § 1.98(b))		IDS Filed	April 8, 2010

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)
Satoh et al., "Medicinal Chemical Studies on Synthetic Protease Inhibitors, trans-4-Guanidinomethylcyclohexanecarboxylic Acid Aryl Esters," Chem. Pharm. Bull. 33:647-654 (1985).
Schechter et al., *On the Size of the Active Site in Proteases. I. Papain,* Biochem. Biophys. Res. Commun. 27:157-162 (1967).
Schmitt et al., "Clinical Impact of the Plasminogen Activation System in Tumor Invasion and Metastasis: Prognostic Relevance and Target for Therapy," <i>Thrombosis and Haemostasis</i> 78:285-296 (1997).
Shi et al., "Identification and Characterization of a Novel Matrix-degrading Protease from Hormone-dependent Human Breast Cancer Cells," Cencer Res. 53:1409-1415 (1993).
Silverberg et al., "Enzymatic activities of activated and zymogen forms of human Hageman factor (factor XII)," Blood 60:84-70 (1982).
Soil et al., "Amidinohydrazones as Guanidine Bioisosteres: Application to a New Class of Potent, Selective and Orally Bioavailable, Non-Amide-Based Small Molecule Thrombin Inhibitors," Bioorgania & Medicinal Chemistry Letters 10:1-4 (2000).
Speri et al., "(4-Aminomethyl) Phenylguanidine Derivates as Nonpeptidic Highly Selective Inhibitors of Human Urokinase," <i>Proc. Natl. Acad. Sci. USA</i> 97:5113-5118 (2000).
Speri et al., "Urethanyl-3-Amidinophenylalanine Derivatives as Inhibitors of Factor Xa. X-Ray Crystal Structure of a Trypsin/Inhibitor Complex and Modeling Studies," Biol. Chem. 381:321-329 (2000).
Stauffer et al., *9-Hydroxyazafluorenes and their Use in Thrombin Inhibitors,* J. Med. Chem., 48: 2282-2293 (2005).
Stephens et al., "The Urokinase Plasminogen Activator System as a Target for Prognostic Studies in Breast Cancer," Breast Cancer Research and Treatment," 52:99-111 (1998).
Stürzebecher et al., "Novel Plasma Kallikrein Inhibitors of the Benzamidine Type," Brazilian Journal Med. Biol. Res. 27:1929-1934 (1994).
Stürzebecher et al., "3-Amidinophenylalanine-Based Inhibitors of Urokinase," <i>Bioorganic & Medicinal Chemistry</i> Letters 9:3147-3152 (1999).
 Stürzebecher et al., "Synthesis and Structure Activity Relationships of Potent Thrombin Inhibitors: Piperazides of 3-Amidinophenylalanine." <i>J. Med. Chem.</i> 40:3091-3099 (1997).
Stürzebecher et al., "Synthetic Inhibitors of Bovine Factor Xa and Thrombin Comparison of Their Anticoagulant Efficiency," <i>Thromb. Res.</i> 54:245-252 (1989).
Stürzebecher et al., Zentralbl. Pharm. Pharmakother. Lab. Diagn. 122:240-241 (1983).

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EXAMINER: Initial citation considered. Draw line through citation	if not in conformance and not considered. Include copy of this

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EXAMINER

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SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE	Attorney Docket No.	50125/102001
(MODIFIED) PATENT AND TRADEMARK OFFICE	Serial No.	10/540,958
	Applicant	Stürzebecher et al.
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	Filing Date	January 3, 2006
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(37 C.F.R. § 1.98(b))	IDS Filed	April 8, 2010

	OTHER DOCUMENTS (INCLUDING AUTHOR, 1	TITLE, DATE, PLACE OF PUBLICATION	TION)	
	Sucker et al., Pharm. Techn. 2., Bauer, Georg Thien	ne Verlag, Stuttgart, (1991).		
	Tada et al., "Isolation of Plasma Kallikrein by High E Biol. Pharm. Bull. 24:520-524 (2001).	fficiency Affinity Chromatography an	d Its Characterization,"	
	Takeuchi et al., "Reverse Blochemistry: Use of Macr Processes and Identify a Membrane-type Serine Pro Acad. Sci. USA 96:11054-11061 (1999).	omolecular Protease Inhibitors to Di otease in Epithelial Cancer and Norm	ssect Complex Biological nal Tissue," Proc. Natl.	
	Takeuchi et al., "Cellular Localization of Membrane- activated Receptor-2 and Single-chain Urokinase-ty 275:26333-26342 (2000).			
	Tamura et al., "Synthesis and Biological Activity of P Medicinal Chemistry Letters, 10:983-987 (2000).	eptidyl Aldehyde Urokinase Inhibitor	s." Bioorganic &	
	Teno et al., "Development of Selective Inhibitors aga (1991).	inst Plasma," Kallikrein Chem. Pha	m. Bull. 39:2930-2936	
	Towle et al., "Inhibition of Urokinase by 4-Substituted Benzolbjthlophene-2-Carboxamidines: An Important Class of Selective Synthetic Urokinase Inhibitor," Cancer Research 53:2553-2559 (1993).			
	Tucker et al., "Potent Noncovalent Thrombin Inhibito in the P3 Position. Implications on Oral Bioavailabilit (1997).			
	Tucker et al., "Synthesis of a Series of Potent and Orally Bioavailable Thrombin Inhibitors That Utilize 3,3- Disubstituted Propionic Acid Derivatives in the P3 Position," <i>J. Med. Chem.</i> 40:3687-3693 (1997). Tsuda et al., Structure-inhibitory Activity Relationship of Plasmin and Plasma Kalilkrein Inhibitors," <i>Chem. Pha Bull.</i> 49:1457-1463 (2001). Vassaili et al., "Arniloride Selectively Inhibits the Urokinase-Type Plasminogen Activator," <i>FEB</i> 214:187-191 (1987).			
	von der Saal et al, "Derivatives of 4-Amino-Pyridine : Chemistry Letters 7:1283-1288 (1997).	as Selective Thrombin Inhibitors," Bi	oorganic & Medicinal	
Wagner et al., "Synthese von N-[Amidinobenzyl]-und N-[Amidinophenyl]-Phthalimide und-1-Ox. Pharmazie 32:76-79 (1977).				
	Weitz, "New Anticoagulants for Treatment of Venous	s Thromboembolism," Circulation, 11	I0:I-19-I-26 (2004).	
	Wikström et al., "Development and Validation of a C Ximelagatran Drug Substances," J. Sep. Sci. 25:116		od for Melagatran and	
EXAMINER	/Marcos Sznaidman/ D/	ATE CONSIDERED	12/02/2010	

SUBSTITUTE FORM PTO-1449 (MODIFIED)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	Attorney Docket No.	50125/102001
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(37 C.F.R. § 1.98(b))		IDS Filed	April 8, 2010

OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PLACE OF PUBLICATION)
Zeslawska et al., "Crystals of the Urokinase Type Plasminogen Activator Variant &c-uPA in Complex with Small Molecule Inhibitors Open the Way towards Structure-based Drug Design," J. Mol. Biol. 301:465-475 (2000).
Zeslawska et al., "Crystals of Urokinase Type Plasminogen Activator Complexes Reveal the Binding Mode of Peptidomimetic Inhibitors," J. Mol. Biol. 328:109-118 (2003).
Zhang et al., "Assignment of Human Putative Tumor Suppressor Genes ST13 (alias SNC6) and ST14 (alias SNC19) to human Chromosome Bands Z2q13 and 11q24—q25 by in Situ Hybridization," Cytogenet Cell Genet. 83:65-57 (1998).
Zhu et al., "Recent Advances in Inhibitors of Factor Xa in the Prothrombinase Complex," Curr. Opin. Cardiovasc. Pulmon. Renal Invest. Drugs 1:63-87 (1999).
Office Action pertaining to U.S. Patent Application No. 10/297,557 mailed November 4, 2003.
Office Action pertaining to U.S. Patent Application No. 10/311,364 mailed November 19, 2003.
Office Action pertaining to U.S. Patent Application No. 10/311,364 mailed April 1, 2004.
Office Action pertaining to U.S. Patent Application No. 10/506,579 mailed December 16, 2009.
Office Action pertaining to U.S. Patent Application No. 10/506,579 mailed January 30, 2009.
Office Action pertaining to U.S. Patent Application No. 10/506,579 mailed July 17, 2008.
Office Action pertaining to U.S. Patent Application No. 10/555,821, mailed January 21, 2009.
Office Action pertaining to U.S. Patent Application No. 10/571,026, mailed December 13, 2007
Office Action pertaining to U.S. Patent Application No. 10/571,026, mailed February 23, 2009
Office Action pertaining to U.S. Patent Application No. 10/571,026, mailed October 30, 2009
International Search Report for International Application No. PCT/EP2004/000247, dated August 18, 2004
International Preliminary Report on Patentability for International Application No. PCT/EP2004/000247, dated September 2, 2005
Written Opinion of the International Search Authority for International Application No. PCT/EP2004/000247, dated August 18, 2004

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